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CLAIMS

- 5
1. A pharmaceutical composition for modulating cholinergic function in a mammal comprising:
- (a) a NRPA compound or a pharmaceutically acceptable salt thereof;
- (b) an anti-emetic/anti-nausea agent or a pharmaceutically acceptable salt thereof;
- 10 and
- (c) a pharmaceutically acceptable carrier;
- wherein the active ingredient (a) and (b) above are present in amounts that render the composition effective in the treatment of a disorder or condition selected from inflammatory bowel disease (including but not limited to ulcerative colitis, pyoderma gangrenosum and
- 15 Crohn's disease), irritable bowel syndrome, spastic dystonia, chronic pain, acute pain, celiac sprue, pouchitis, vasoconstriction, anxiety, panic disorder, depression, bipolar disorder, autism, sleep disorders, jet lag, amyotrophic lateral sclerosis (ALS), cognitive dysfunction, hypertension, bulimia, anorexia, obesity, cardiac arrhythmias, gastric acid hypersecretion, ulcers, pheochromocytoma, progressive supranuclear palsy, chemical dependencies and
- 20 addictions (e.g., dependencies on, or addictions to nicotine (and/or tobacco products), alcohol, benzodiazepines, barbiturates, opioids or cocaine), headache, migraine, stroke, traumatic brain injury (TBI), obsessive-compulsive disorder (OCD), psychosis, Huntington's chorea, tardive dyskinesia, hyperkinesia, dyslexia, schizophrenia, multi-infarct dementia, age-related cognitive decline, epilepsy, including petit mal absence epilepsy, senile dementia of
- 25 the Alzheimer's type (AD), Parkinson's disease (PD), attention deficit hyperactivity disorder (ADHD) and Tourette's Syndrome.
2. A pharmaceutical composition as recited in claim 1 wherein the NRPA compound is selected from:
- 9-bromo-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
- 30 9-chloro-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
- 9-flouro-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
- 9-ethyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
- 9-methyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
- 9-phenyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
- 35 9-vinyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
- 9-bromo-3-methyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;

- 5 3-benzyl-9-bromo-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
 3-benzyl-9-chloro-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
 9-acetyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
10 9-iodo-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
 9-cyano-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
 9-ethynyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
 9-(2-propenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
 9-(2-propyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
15 9-carbomethoxy-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
 9-carboxyaldehyde-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
 9-(2,6-difluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
20 9-phenyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
 9-(2-fluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
 9-(4-fluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
25 9-(3-fluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
 9-(3,5-difluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
 9-(2,4-difluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
30 9-(2,5-difluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
 6-methyl-5-oxo-6,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,8-triene;
 5-oxo-6,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,8-triene;
35 6-oxo-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,8-triene;
 4,5-difluoro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
 5-fluoro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene-4-carbonitrile;
 4-ethynyl-5-fluoro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;

- 5 5-ethynyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene-4-carbonitrile;
6-methyl-5-thia-5-dioxa-6,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,8-
triene;
- 10 10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
4-fluoro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
4-methyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
4-trifluoromethyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
4-nitro-10-azatetracyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
7-methyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-tetraene;
6-methyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-tetraene;
- 15 6,7-dimethyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-tetraene;
6-methyl-7-phenyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-
tetraene;
- 20 6,7-dimethyl-5,8,14-triazatetracyclo[10.3.1.0^{2,11}.0^{4,9}]hexadeca-2(11),3,5,7,9-pentaene;
5,8,14-triazatetracyclo[10.3.1.0^{2,11}.0^{4,9}]hexadeca-2(11),3,5,7,9-pentaene;
14-methyl-5,8,14-triazatetracyclo[10.3.1.0^{2,11}.0^{4,9}]hexadeca-2(11),3,5,7,9-pentaene;
5-oxa-7,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,6,8-tetraene;
6-methyl-5-oxa-7,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,6,8-tetraene;
4-chloro-10-azatetracyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
10-azatetracyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-trien-4-yl cyanide;
- 25 1-(10-azatetracyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-trien-4-yl)-1-ethanone;
10-azatetracyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-trien-4-ol;
7-methyl-5-oxa-6,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2,4(8),6,9-tetraene;
4,5-dichloro-10-azatetracyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
11-azatetracyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-5-carbonitrile;
- 30 1-[11-azatetracyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-5-yl]-1-ethanone;
1-[11-azatetracyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-5-yl]-1-propanone;
4-fluoro-11-azatetracyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-5-carbonitrile;
5-fluoro-11-azatetracyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-4-carbonitrile;
6-methyl-7-thia-5,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
- 35 6-methyl-5,7,14-triazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
6,7-dimethyl-5,7,14-triazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
5,7,14-triazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
5,6-dimethyl-5,7,14-triazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,6,8-tetraene;

- 5 5-methyl-5,7,14-triazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,6,8-tetraene;
6-(trifluoromethyl)-7-thia-5,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-
tetraene;
5,8,15-triazatetracyclo[11.3.1.0^{2,11}.0^{4,9}]heptadeca-2(11),3,5,7,9-pentaene;
7-methyl-5,8,15-triazatetracyclo[11.3.1.0^{2,11}.0^{4,9}]heptadeca-2(11),3,5,7,9-pentaene;
10 6-methyl-5,8,15-triazatetracyclo[11.3.1.0^{2,11}.0^{4,9}]heptadeca-2(11),3,5,7,9-pentaene;
6,7-dimethyl-5,8,15-triazatetracyclo[11.3.1.0^{2,11}.0^{4,9}]heptadeca-2(11),3,5,7,9-
pentaene;
7-oxa-5,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
6-methyl-7-oxa-5,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
15 5-methyl-7-oxa-6,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
6-methyl-5-oxa-7,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,6,8-tetraene;
7-methyl-5-oxa-6,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,6,8-tetraene;
4,5-difluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
4-chloro-5-fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
20 5-chloro-4-fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
4-(1-ethynyl)-5-fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
5-(1-ethynyl)-4-fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
5,6-difluoro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene;
6-trifluoromethyl-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene;
25 6-methoxy-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-6-ol;
6-fluoro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-5-ol;
4-nitro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
30 5-nitro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
5-fluoro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
6-hydroxy-5-methoxy-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene and
their pharmaceutically acceptable salts and their optical isomers.
3. A pharmaceutical composition as recited in claim 2 wherein the NRPA
35 compound is selected from the group consisting of:
9-bromo-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-chloro-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-flouro-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;

- 5 9-acetyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
9-iodo-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
9-cyano-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
9-carbomethoxy-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
9-carboxyaldehyde-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-
10 one;
9-(2,6-difluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-
one;
9-phenyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
9-(2-fluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-
15 one;
6-methyl-5-thia-5-dioxa-6,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,8-
triene;
4-fluoro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
4-trifluoromethyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
20 4-nitro-10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
6-methyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-tetraene;
6,7-dimethyl-5,8,14-triazatetracyclo[10.3.1.0^{2,11}.0^{4,9}]hexadeca-2(11),3,5,7,9-pentaene;
5,8,14-triazatetracyclo[10.3.1.0^{2,11}.0^{4,9}]hexadeca-2(11),3,5,7,9-pentaene;
5-oxa-7,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,6,8-tetraene;
25 6-methyl-5-oxa-7,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,6,8-tetraene;
10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-trien-4-yl cyanide;
1-(10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-trien-4-yl)-1-ethanone;
11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-5-carbonitrile;
1-[11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-5-yl]-1-ethanone;
30 1-[11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-5-yl]-1-propanone;
4-fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-5-carbonitrile;
5-fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-4-carbonitrile;
6-methyl-7-thia-5,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
6-methyl-5,7,14-triazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
35 6,7-dimethyl-5,7,14-triazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
6-methyl-7-oxa-5,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
6-methyl-5-oxa-7,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,6,8-tetraene;
5,6-difluoro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene;

5 6-trifluoromethyl-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene;
6-methoxy-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
6-fluoro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-5-ol and
their pharmaceutically acceptable salts and their optical isomers.

10 4. A pharmaceutical composition according to claim 1 wherein the anti-
emetic/anti-nausea agent is selected from the group consisting of: bismuth subsalicylate
(Pepto-Bismol), chlorpromazine (Thorazine), dextrose/levulose/phosphoric acid (Emetrol),
dimenhydrinate (Dramamine), diphenhydramine (Benadryl), dolasetron (Anzemet), dronabinol
(Marinol), granisetron (Kytril), hydroxyzine (Atarax/Vistaril), meclizine (Antivert/Bonine),
15 metoclopramide (Reglan), ondansetron (Zofran), perphenazine (Trilafon), prochlorperazine
(Compazine), promethazine (Phenergan), scopolamine (Transderm Scop),
trimethobenzamide (Tigan).

5. A pharmaceutical composition according to Claim 1 wherein the anti-
emetic/anti-nausea agent is selected from the group consisting of:

20 (2S,3S)-3-(5-tert-butyl-2-methoxybenzyl)amino-2-(3-trifluoromethoxyphenyl)piperidine;
(2S,3S)-3-(2-isopropoxy-5-trifluoromethoxybenzyl)amino-2-phenylpiperidine;
(2S,3S)-3-(2-ethoxy-5-trifluoromethoxybenzyl)amino-2-phenylpiperidine;
(2S,3S)-3-(2-methoxy-5-trifluoromethoxybenzyl)-amino-2-phenylpiperidine;
(2S,3S)-3-(5-tert-butyl-2-trifluoromethoxybenzyl)amino-2-phenylpiperidine;
25 2-(diphenylmethyl)-N-(2-methoxy-5-trifluoromethoxy-phenyl)methyl-1-
azabicyclo[2.2.2]octan-3-amine;
(2S,3S)-3-[5-chloro-2-(2,2,2-trifluoroethoxy)-benzyl]amino-2-phenylpiperidine;
(2S,3S)-3-(5-tert-butyl-2-trifluoromethoxybenzyl)amino-2-phenylpiperidine;
(2S,3S)-3-(2-isopropoxy-5-trifluoromethoxybenzyl)amino-2-phenylpiperidine;
30 (2S,3S)-3-(2-difluoromethoxy-5-trifluoromethoxybenzyl)-amino-2-phenylpiperidine;
(2S,3S)-2-phenyl-3-[2-(2,2,2-trifluoroethoxybenzyl)-aminopiperidine; or
(2S,3S)-2-phenyl-3-(2-trifluoromethoxybenzyl)]aminopiperidine;
3-[N-(2-methoxy-5-trifluoromethoxybenzyl)-amino]-5,5-dimethyl-2-phenylpyrrolidine;
3-[N-(2-methoxy-5-trifluoromethoxy-benzyl)amino]-4,5-dimethyl-2-phenylpyrrolidine;
35 3-(2-cyclopropyloxy-5-trifluoromethoxybenzyl)amino-2-phenylpiperidine;
3-(2-cyclopropylmethoxy-5-trifluoromethoxybenzyl)amino-2-phenylpiperidine;
3-(2-difluoromethoxy-5-phenylbenzyl)amino-2-phenylpiperidine;
3-(5-cyclopropylmethoxy-2-difluoromethoxybenzyl)amino-2-phenylpiperidine;

- 5 3-(2-methoxybenzyl)amino-2-(3-trifluoromethoxyphenyl)-piperidine;
3-(2-methoxy-5-trifluoromethoxybenzyl)amino-2-(3-trifluoromethoxyphenyl)piperidine;
2-phenyl-3-(5-n-propyl-2-trifluoromethoxybenzyl)amino-piperidine;
3-(5-isopropyl-2-trifluoromethoxybenzyl)amino-2-phenylpiperidine;
3-(5-ethyl-2-trifluoromethoxybenzyl)amino-2-phenyl-piperidine;
10 3-(5-sec-butyl-2-trifluoromethoxybenzyl)amino-2-phenyl-piperidine;
3-(5-difluoromethoxy-2-methoxybenzyl)amino-2-phenyl-piperidine;
3-(2-methoxy-5-trifluoromethoxybenzyl)amino-2-phenylpyrrolidine;
3-(2-methoxy-5-trifluoromethoxybenzyl)amino-2-phenylhomopiperidine;
2-benzhydryl-3-(2-methoxy-5-trifluoromethoxy-benzyl)aminopyrrolidine;
15 2-benzhydryl-3-(2-methoxy-5-trifluoromethoxy-benzyl)aminohomopiperidine;
3-[2,5-bis-(2,2,2-trifluoroethoxy)benzyl]amino-2-phenylpiperidine;
(2-Methoxy-5-trifluoromethoxy-benzyl)-(2-phenyl-piperidin-3-yl)-amine;
5-[(6-Ethyl-2-phenyl-piperidin-3-ylamino)-methyl]-6-methoxy-3-methyl-1,1a,3,7b-
tetrahydro-3-aza-cyclopropa[a]naphthalen-2-one;
20 (6-Methoxy-1-methyl-1-trifluoromethyl-isochroman-7-ylmethyl)-(2-phenyl-piperidin-3-
yl)-amine;
2-phenyl-3-(3-trifluoromethoxybenzyl)aminopiperidine;
2-benzhydryl-3-(2-methoxy-5-trifluoromethoxybenzyl)-aminopiperidine;
1-(5,6-difluorohexyl)-3-(2-methoxy-5-trifluoromethoxy-benzyl)amino-2-phenylpiperidine;
25 1-(6-hydroxyhexyl)-3-(2-methoxy-5-trifluoromethoxy-benzyl)amino-2-phenylpiperidine;
3-phenyl-4-(2-methoxy-5-trifluoromethoxybenzyl)amino-2-azabicyclo[3.3.0]octane;
4-benzhydryl-5-(2-methoxy-5-trifluoromethoxybenzyl)-amino-3-
azabicyclo[4.1.0]heptane;
4-(2-methoxy-5-trifluoromethoxybenzyl)amino-3-phenyl-2-azabicyclo[4.4.0]decane;
30 2-phenyl-3-(2-methoxy-5-trifluoromethoxybenzyl)-aminoquinuclidine;
8-benzhydryl-N-(2-methoxy-5-trifluoromethoxybenzyl)-9-azatricyclo[4.3.1.0^{4,9}]decan-7-
amine;
9-benzhydryl-N-(2-methoxy-5-trifluoromethoxybenzyl)-10-
azatricyclo[4.4.1.0^{5,10}]undecan-8-amine;
35 9-benzhydryl-N-(2-methoxy-5-trifluoromethoxybenzyl)-3-thia-10-azatricyclo-
[4.4.1.0^{5,10}]undecan-8-amine;
8-benzhydryl-N-(2-methoxy-5-trifluoromethoxybenzyl)-9-azatricyclo[4.3.1.0^{4,9}]decan-7-
amine;

- 5 5,6-pentamethylene-2-benzhydryl-3-(2-methoxy-5-trifluoromethoxybenzyl)amino-
quinuclidine;
 5,6-trimethylene-2-benzhydryl-3-(2-methoxy-5-trifluoromethoxybenzyl)amino-
quinuclidine;
 9-benzhydryl-N-((2-methoxy-5-trifluoromethoxyphenyl)-methyl)-3-oxa-10-azatricyclo-
10 [4.4.1.0^{5,10}]undecan-3-amine;
 8-benzhydryl-N-((2-methoxy-5-trifluoromethoxyphenyl)-methyl)-7-azatricyclo-
[4.4.1.0^{5,10}]undecan-9-amine; and
 2-benzhydryl-N-((2-methoxy-5-trifluoromethoxyphenyl)-methyl)-1-azabicyclo-
[3.2.2]nonan-3-amine;
15 (2S,3S)-3-(6-methoxy-1-methyl-1-trifluoromethylisochroman-7-yl)methylamino-2-
phenylpiperidine;
 (2S,3S)-3-[(1R)-6-methoxy-1-methyl-1-trifluoromethylisochroman-7-yl]methylamino-2-
phenylpiperidine;
 (2S,3S)-N-(5-isopropyl-2-methoxyphenyl)methyl-2-diphenylmethyl-1-azabicyclo[2.2.2]-
20 octan-3-amine; and
 (2S,3S)-N-(5-tert-butyl-2-methoxyphenyl)-methyl-2-diphenylmethyl-1-azabicyclo[2.2.2]-
octan-3-amine;
 and their pharmaceutically acceptable salts.
6. A method of modulating cholinergic function in a mammal comprising
25 administering to said mammal, an amount of
 (a) a NRPA compound or a pharmaceutically acceptable salt thereof; and
 (b) an anti-emetic/anti-nausea agent;
 wherein the active ingredients (a) and (b) are administered in amounts that render the
combination of the two ingredients effective in the treatment of a disorder or condition selected
30 from inflammatory bowel disease (including but not limited to ulcerative colitis, pyoderma
gangrenosum and Crohn's disease), irritable bowel syndrome, spastic dystonia, chronic pain,
acute pain, celiac sprue, pouchitis, vasoconstriction, anxiety, panic disorder, depression,
bipolar disorder, autism, sleep disorders, jet lag, amyotrophic lateral sclerosis (ALS), cognitive
dysfunction, hypertension, bulimia, anorexia, obesity, cardiac arrhythmias, gastric acid
35 hypersecretion, ulcers, pheochromocytoma, progressive supranuclear palsy, chemical
dependencies and addictions (e.g., dependencies on, or addictions to nicotine (and/or
tobacco products), alcohol, benzodiazepines, barbiturates, opioids or cocaine), headache,
migraine, stroke, traumatic brain injury (TBI), obsessive-compulsive disorder (OCD),

5 psychosis, Huntington's chorea, tardive dyskinesia, hyperkinesia, dyslexia, schizophrenia, multi-infarct dementia, age-related cognitive decline, epilepsy, including petit mal absence epilepsy, senile dementia of the Alzheimer's type (AD), Parkinson's disease (PD), attention deficit hyperactivity disorder (ADHD) and Tourette's Syndrome.

7. A method as recited in claim 6 wherein the NRPA compound is selected from:

10 9-bromo-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-chloro-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-flouro-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-ethyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-methyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
15 9-phenyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-vinyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-bromo-3-methyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
one;
3-benzyl-9-bromo-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
20 one;
3-benzyl-9-chloro-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
one;
9-acetyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
9-iodo-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
25 9-cyano-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
9-ethynyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
9-(2-propenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
9-(2-propyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
9-carbomethoxy-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
30 9-carboxyaldehyde-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
one;
9-(2,6-difluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
one;
9-phenyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
35 9-(2-fluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
one;
9-(4-fluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
one;

- 5 9-(3-fluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
9-(3,5-difluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
9-(2,4-difluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
10 9-(2,5-difluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
6-methyl-5-oxo-6,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,8-triene;
5-oxo-6,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,8-triene;
15 6-oxo-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,8-triene;
4,5-difluoro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
5-fluoro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene-4-carbonitrile;
4-ethynyl-5-fluoro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
5-ethynyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene-4-carbonitrile;
20 6-methyl-5-thia-5-dioxa-6,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,8-triene;
10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
4-fluoro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
4-methyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
25 4-trifluoromethyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
4-nitro-10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
7-methyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-tetraene;
6-methyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-tetraene;
6,7-dimethyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-tetraene;
30 6-methyl-7-phenyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-tetraene;
6,7-dimethyl-5,8,14-triazatetracyclo[10.3.1.0^{2,11}.0^{4,9}]hexadeca-2(11),3,5,7,9-pentaene;
5,8,14-triazatetracyclo[10.3.1.0^{2,11}.0^{4,9}]hexadeca-2(11),3,5,7,9-pentaene;
14-methyl-5,8,14-triazatetracyclo[10.3.1.0^{2,11}.0^{4,9}]hexadeca-2(11),3,5,7,9-pentaene;
35 5-oxa-7,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,6,8-tetraene;
6-methyl-5-oxa-7,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,6,8-tetraene;
4-chloro-10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-trien-4-yl cyanide;

- 5 1-(10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-trien-4-yl)-1-ethanone;
10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-trien-4-ol;
7-methyl-5-oxa-6,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2,4(8),6,9-tetraene;
4,5-dichloro-10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-5-carbonitrile;
- 10 1-[11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-5-yl]-1-ethanone;
1-[11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-5-yl]-1-propanone;
4-fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-5-carbonitrile;
5-fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-4-carbonitrile;
- 15 6-methyl-7-thia-5,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
6-methyl-5,7,14-triazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
6,7-dimethyl-5,7,14-triazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
5,7,14-triazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
5,6-dimethyl-5,7,14-triazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,6,8-tetraene;
5-methyl-5,7,14-triazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,6,8-tetraene;
- 20 6-(trifluoromethyl)-7-thia-5,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
5,8,15-triazatetracyclo[11.3.1.0^{2,11}.0^{4,9}]heptadeca-2(11),3,5,7,9-pentaene;
7-methyl-5,8,15-triazatetracyclo[11.3.1.0^{2,11}.0^{4,9}]heptadeca-2(11),3,5,7,9-pentaene;
6-methyl-5,8,15-triazatetracyclo[11.3.1.0^{2,11}.0^{4,9}]heptadeca-2(11),3,5,7,9-pentaene;
- 25 6,7-dimethyl-5,8,15-triazatetracyclo[11.3.1.0^{2,11}.0^{4,9}]heptadeca-2(11),3,5,7,9-pentaene;
7-oxa-5,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
6-methyl-7-oxa-5,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
5-methyl-7-oxa-6,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
- 30 6-methyl-5-oxa-7,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,6,8-tetraene;
7-methyl-5-oxa-6,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,6,8-tetraene;
4,5-difluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
4-chloro-5-fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
5-chloro-4-fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
- 35 4-(1-ethynyl)-5-fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
5-(1-ethynyl)-4-fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
5,6-difluoro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene;
6-trifluoromethyl-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene;

- 5 6-methoxy-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-6-ol;
6-fluoro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-5-ol;
4-nitro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
10 5-nitro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
5-fluoro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
6-hydroxy-5-methoxy-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene and
their pharmaceutically acceptable salts and their optical isomers.
8. The method of claim 6 wherein the NRPA compound is selected from:
- 15 9-bromo-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-chloro-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-flouro-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-acetyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-iodo-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
20 9-cyano-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-carbomethoxy-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-carboxyaldehyde-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-
one;
9-(2,6-difluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-
25 one;
9-phenyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-(2-fluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-
one;
6-methyl-5-thia-5-dioxa-6,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,8-
30 triene;
4-fluoro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
4-trifluoromethyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
4-nitro-10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
6-methyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-tetraene;
35 6,7-dimethyl-5,8,14-triazatetracyclo[10.3.1.0^{2,11}.0^{4,9}]hexadeca-2(11),3,5,7,9-pentaene;
5,8,14-triazatetracyclo[10.3.1.0^{2,11}.0^{4,9}]hexadeca-2(11),3,5,7,9-pentaene;
5-oxa-7,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,6,8-tetraene;
6-methyl-5-oxa-7,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,6,8-tetraene;

- 5 10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-trien-4-yl cyanide;
1-(10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-trien-4-yl)-1-ethanone;
11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-5-carbonitrile;
1-[11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-5-yl]-1-ethanone;
1-[11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-5-yl]-1-propanone;
- 10 4-fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-5-carbonitrile;
5-fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-4-carbonitrile;
6-methyl-7-thia-5,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
6-methyl-5,7,14-triazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
6,7-dimethyl-5,7,14-triazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
- 15 6-methyl-7-oxa-5,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
6-methyl-5-oxa-7,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,6,8-tetraene;
5,6-difluoro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene;
6-trifluoromethyl-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene;
6-methoxy-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
- 20 6-fluoro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-5-ol and
their pharmaceutically acceptable salts and their optical isomers.

9. A method according to claim 6 wherein the anti-emetic/anti-nausea agent is selected from the group consisting of:

- 25 bismuth subsalicylate (Pepto-Bismol), chlorpromazine (Thorazine),
dextrose/levulose/phosphoric acid (Emetrol), dimenhydrinate (Dramamine), diphenhydramine
(Benadryl), dolasetron (Anzemet), dronabinol (Marinol), granisetron (Kytrel), hydroxyzine
(Atarax/Vistaril), meclizine (Antivert/Bonine), metoclopramide (Reglan), ondansetron (Zofran),
perphenazine (Trilafon), prochlorperazine (Compazine), promethazine (Phenergan),
30 scopolamine (Transderm Scop), trimethobenzamide (Tigan).

10. A method according to Claim 6 wherein the anti-emetic/anti-nausea agent is selected from the group consisting of:

- (2S,3S)-3-(5-tert-butyl-2-methoxybenzyl)amino-2-(3-trifluoromethoxyphenyl)piperidine;
(2S,3S)-3-(2-isopropoxy-5-trifluoromethoxybenzyl)amino-2-phenyl-piperidine;
- 35 (2S,3S)-3-(2-ethoxy-5-trifluoromethoxybenzyl)amino-2-phenyl-piperidine;
(2S,3S)-3-(2-methoxy-5-trifluoromethoxybenzyl)-amino-2-phenylpiperidine;
(2S,3S)-3-(5-tert-butyl-2-trifluoromethoxybenzyl)amino-2-phenylpiperidine;

- 5 2-(diphenylmethyl)-N-(2-methoxy-5-trifluoromethoxy-phenyl)methyl-1-
azabicyclo[2.2.2]octan-3-amine;
 (2S,3S)-3-[5-chloro-2-(2,2,2-trifluoroethoxy)-benzyl]amino-2-phenylpiperidine;
 (2S,3S)-3-(5-tert-butyl-2-trifluoromethoxybenzyl)amino-2-phenylpiperidine;
 (2S,3S)-3-(2-isopropoxy-5-trifluoromethoxybenzyl)amino-2-phenylpiperidine;
10 (2S,3S)-3-(2-difluoromethoxy-5-trifluoromethoxybenzyl)-amino-2-phenylpiperidine;
 (2S,3S)-2-phenyl-3-[2-(2,2,2-trifluoroethoxybenzyl)-aminopiperidine; or
 (2S,3S)-2-phenyl-3-(2-trifluoromethoxybenzyl)]aminopiperidine;
 3-[N-(2-methoxy-5-trifluoromethoxybenzyl)-amino]-5,5-dimethyl-2-phenylpyrrolidine;
 3-[N-(2-methoxy-5-trifluoromethoxy-benzyl)amino]-4,5-dimethyl-2-phenylpyrrolidine;
15 3-(2-cyclopropyloxy-5-trifluoromethoxybenzyl)amino-2-phenylpiperidine;
 3-(2-cyclopropylmethoxy-5-trifluoromethoxybenzyl)amino-2-phenylpiperidine;
 3-(2-difluoromethoxy-5-phenylbenzyl)amino-2-phenylpiperidine;
 3-(5-cyclopropylmethoxy-2-difluoromethoxybenzyl)amino-2-phenylpiperidine;
 3-(2-methoxybenzyl)amino-2-(3-trifluoromethoxyphenyl)-piperidine;
20 3-(2-methoxy-5-trifluoromethoxybenzyl)amino-2-(3-tri-fluoromethoxyphenyl)piperidine;
 2-phenyl-3-(5-n-propyl-2-trifluoromethoxybenzyl)amino-piperidine;
 3-(5-isopropyl-2-trifluoromethoxybenzyl)amino-2-phenylpiperidine;
 3-(5-ethyl-2-trifluoromethoxybenzyl)amino-2-phenyl-piperidine;
 3-(5-sec-butyl-2-trifluoromethoxybenzyl)amino-2-phenyl-piperidine;
25 3-(5-difluoromethoxy-2-methoxybenzyl)amino-2-phenyl-piperidine;
 3-(2-methoxy-5-trifluoromethoxybenzyl)amino-2-phenylpyrrolidine;
 3-(2-methoxy-5-trifluoromethoxybenzyl)amino-2-phenylhomopiperidine;
 2-benzhydryl-3-(2-methoxy-5-trifluoromethoxy-benzyl)aminopyrrolidine;
 2-benzhydryl-3-(2-methoxy-5-trifluoromethoxy-benzyl)aminohomopiperidine;
30 3-[2,5-bis-(2,2,2-trifluoroethoxy)benzyl]amino-2-phenylpiperidine;
 (2-methoxy-5-trifluoromethoxy-benzyl)-(2-phenyl-piperidin-3-yl)-amine;
 5-[(6-ethyl-2-phenyl-piperidin-3-ylamino)-methyl]-6-methoxy-3-methyl-1,1a,3,7b-
tetrahydro-3-aza-cyclopropa[a]naphthalen-2-one;
 (6-methoxy-1-methyl-1-trifluoromethyl-isochroman-7-ylmethyl)-(2-phenyl-piperidin-3-
35 yl)-amine;
 2-phenyl-3-(3-trifluoromethoxybenzyl)aminopiperidine;
 2-benzhydryl-3-(2-methoxy-5-trifluoromethoxybenzyl)-aminopiperidine;
 1-(5,6-difluorohexyl)-3-(2-methoxy-5-trifluoromethoxy-benzyl)amino-2-phenylpiperidine;

- 5 1-(6-hydroxyhexyl)-3-(2-methoxy-5-trifluoromethoxy-benzyl)amino-2-phenylpiperidine;
 3-phenyl-4-(2-methoxy-5-trifluoromethoxybenzyl)amino-2-azabicyclo[3.3.0]octane;
 4-benzhydryl-5-(2-methoxy-5-trifluoromethoxybenzyl)-amino-3-
 azabicyclo[4.1.0]heptane;
 4-(2-methoxy-5-trifluoromethoxybenzyl)amino-3-phenyl-2-azabicyclo[4.4.0]decane;
10 2-phenyl-3-(2-methoxy-5-trifluoromethoxybenzyl)-aminoquinuclidine;
 8-benzhydryl-N-(2-methoxy-5-trifluoromethoxybenzyl)-9-azatricyclo[4.3.1.0^{4,9}]decan-7-
 amine;
 9-benzhydryl-N-(2-methoxy-5-trifluoromethoxybenzyl)-10-
 azatricyclo[4.4.1.0^{5,10}]undecan-8-amine;
15 9-benzhydryl-N-(2-methoxy-5-trifluoromethoxybenzyl)-3-thia-10-azatricyclo-
 [4.4.1.0^{5,10}]undecan-8-amine;
 8-benzhydryl-N-(2-methoxy-5-trifluoromethoxybenzyl)-9-azatricyclo[4.3.1.0^{4,9}]decan-7-
 amine;
 5,6-pentamethylene-2-benzhydryl-3-(2-methoxy-5-trifluoromethoxybenzyl)amino-
20 quinuclidine;
 5,6-trimethylene-2-benzhydryl-3-(2-methoxy-5-trifluoromethoxybenzyl)amino-
 quinuclidine;
 9-benzhydryl-N-((2-methoxy-5-trifluoromethoxyphenyl)-methyl)-3-oxa-10-azatricyclo-
 [4.4.1.0^{5,10}]undecan-3-amine;
25 8-benzhydryl-N-((2-methoxy-5-trifluoromethoxyphenyl)-methyl)-7-azatricyclo-
 [4.4.1.0^{5,10}]undecan-9-amine; and
 2-benzhydryl-N-((2-methoxy-5-trifluoromethoxyphenyl)-methyl)-1-azabicyclo-
 [3.2.2]nonan-3-amine;
 (2S,3S)-3-(6-methoxy-1-methyl-1-trifluoromethylisochroman-7-yl)methylamino-2-
30 phenylpiperidine;
 (2S,3S)-3-[(1R)-6-methoxy-1-methyl-1-trifluoromethylisochroman-7-yl]methylamino-2-
 phenylpiperidine;
 (2S,3S)-N-(5-isopropyl-2-methoxyphenyl)methyl-2-diphenylmethyl-1-azabicyclo[2.2.2]-
 octan-3-amine; and
35 (2S,3S)-N-(5-tert-butyl-2-methoxyphenyl)-methyl-2-diphenylmethyl-1-azabicyclo[2.2.2]-
 octan-3-amine;
 and their pharmaceutically acceptable salts.

5 11. A method according to claim 6 wherein the NRPA compound and the anti-emetic/anti-nausea agent are administered substantially simultaneously.

12. A pharmaceutical composition for modulating cholinergic function and treating a disorder or condition selected from inflammatory bowel disease (including but not limited to ulcerative colitis, pyoderma gangrenosum and Crohn's disease), irritable bowel syndrome, spastic dystonia, chronic pain, acute pain, celiac sprue, pouchitis, vasoconstriction, anxiety, panic disorder, depression, bipolar disorder, autism, sleep disorders, jet lag, amyotrophic lateral sclerosis (ALS), cognitive dysfunction, hypertension, bulimia, anorexia, obesity, cardiac arrhythmias, gastric acid hypersecretion, ulcers, pheochromocytoma, progressive supranuclear palsy, chemical dependencies and addictions (e.g., dependencies on, or addictions to nicotine
10 (and/or tobacco products), alcohol, benzodiazepines, barbiturates, opioids or cocaine), headache, migraine, stroke, traumatic brain injury (TBI), obsessive-compulsive disorder (OCD), psychosis, Huntington's chorea, tardive dyskinesia, hyperkinesia, dyslexia, schizophrenia, multi-infarct dementia, age-related cognitive decline, epilepsy, including petit mal absence epilepsy, senile dementia of the Alzheimer's type (AD), Parkinson's disease
15 (PD), attention deficit hyperactivity disorder (ADHD) and Tourette's Syndrome comprising administering to said mammal:

- (a) a NRPA compound or a pharmaceutically acceptable salt thereof;
 - (b) an anti-emetic/anti-nausea agent or a pharmaceutically acceptable salt thereof;
 - 25 (c) a pharmaceutically acceptable carrier,
- wherein (a) and (b) are present in amounts that render the composition effective in treating such disorders and conditions.

13. A method of treating a disorder or condition selected from the group consisting inflammatory bowel disease (including but not limited to ulcerative colitis, pyoderma gangrenosum and Crohn's disease), irritable bowel syndrome, spastic dystonia, chronic pain, acute pain, celiac sprue, pouchitis, vasoconstriction, anxiety, panic disorder, depression, bipolar disorder, autism, sleep disorders, jet lag, amyotrophic lateral sclerosis (ALS), cognitive dysfunction, hypertension, bulimia, anorexia, obesity, cardiac arrhythmias, gastric acid hypersecretion, ulcers, pheochromocytoma, progressive supranuclear palsy, chemical
30 dependencies and addictions (e.g., dependencies on, or addictions to nicotine (and/or tobacco products), alcohol, benzodiazepines, barbiturates, opioids or cocaine), headache, migraine, stroke, traumatic brain injury (TBI), obsessive-compulsive disorder (OCD), psychosis, Huntington's chorea, tardive dyskinesia, hyperkinesia, dyslexia, schizophrenia,
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5 multi-infarct dementia; age-related cognitive decline, epilepsy, including petit mal absence epilepsy, senile dementia of the Alzheimer's type (AD), Parkinson's disease (PD), attention deficit hyperactivity disorder (ADHD) and Tourette's Syndrome comprising administering to said mammal;

(a) a NRPA compound or a pharmaceutically acceptable salt thereof;

10 (b) an anti-emetic/anti-nausea agent or a pharmaceutically acceptable salt thereof; and

wherein the active agents (a) and (b) above are administered in amounts that render the combination of the two ingredients effective in treating such disorders and conditions.